UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/647,067	09/25/2000	Aaron J. W. Hsueh	EL539 356 27	3881

24353 7590 11/12/2003

BOZICEVIC, FIELD & FRANCIS LLP
200 MIDDLEFIELD RD
SUITE 200
MENLO PARK, CA 94025

EXAMINER	
BUNNER, BRIDGET E	
ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 11/12/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Advisory Action	Application No.	Applicant(s)	
	09/647,067	HSUEH ET AL.	
	Examiner	Art Unit	
	Bridget E. Bunner	1647	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 22 October 2003 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE. Therefore, further action by the applicant is required to avoid abandonment of this application. A proper reply to a final rejection under 37 CFR 1.113 may only be either: (1) a timely filed amendment which places the application in condition for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) a timely filed Request for Continued Examination (RCE) in compliance with 37 CFR 1.114.

PERIOD FOR REPLY [check either a) or b)]

a) ☐ The period for reply expires _____months from the mailing date of the final rejection.

b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection. ONLY CHECK THIS BOX WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

1.☒ A Notice of Appeal was filed on *22 October 2003*. Appellant's Brief must be filed within the period set forth in 37 CFR 1.192(a), or any extension thereof (37 CFR 1.191(d)), to avoid dismissal of the appeal.

2.☐ The proposed amendment(s) will not be entered because:

(a) ☐ they raise new issues that would require further consideration and/or search (see NOTE below);

(b) ☐ they raise the issue of new matter (see Note below);

(c) ☐ they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or

(d) ☐ they present additional claims without canceling a corresponding number of finally rejected claims.

NOTE: _____.

3.☒ Applicant's reply has overcome the following rejection(s): See Continuation Sheet.

4.☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).

5.☒ The a)☐ affidavit, b)☐ exhibit, or c)☒ request for reconsideration has been considered but does NOT place the application in condition for allowance because: *See Continuation Sheet.*

6.☐ The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.

7.☒ For purposes of Appeal, the proposed amendment(s) a)☐ will not be entered or b)☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

The status of the claim(s) is (or will be) as follows:

Claim(s) allowed: _____.

Claim(s) objected to: _____.

Claim(s) rejected: *1,2,4,7-11 and 18-20*.

Claim(s) withdrawn from consideration: _____.

8.☒ The drawing correction filed on *22 October 2003* is a)☒ approved or b)☐ disapproved by the Examiner.

9.☐ Note the attached Information Disclosure Statement(s)(PTO-1449) Paper No(s). _____.

10.☒ Other: *Note the attached Interview Summary from 09 October 2003*

Continuation of 3. Applicant's reply has overcome the following rejection(s): The Applicant's response to the Notice to Comply with Sequence Listing Requirements under 37 CFR §1.821 (22 October 2003) has been considered and is found persuasive. The objections to claims 1-2, 4, and 7 are withdrawn in view of the claim amendments (22 October 2003). The rejection of claim 7 under 35 U.S.C. § 112, second paragraph is withdrawn in view of the claim amendments (22 October 2003)

Continuation of 5. does NOT place the application in condition for allowance because: Claims 1-2, 4, 7-11, and 18-20 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a credible, specific and substantial asserted utility or a well established utility. Novel biological molecules lack well established utility and must undergo extensive experimentation. Claims 1-2, 4, 7-11, and 18-20 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Applicant's arguments have been fully considered but are not found to be persuasive. Specifically, although the specification of the instant application teaches that LGR-7 has an ectodomain, there is no disclosure of the location of the ectodomain within LGR-7's amino acid sequence or as to how long it is. It is noted that LGR-7 is not shown in Figure 6 of the instant application and there is no indication that LGR-7 ectodomain is 300 amino acids in length. Additionally, although Applicant argues that the asserted utility an amino-terminal ectodomain that can be expressed as soluble proteins and used to neutralize the activity of an endogenous hormone ligand is specific to LGR-type GPCR, this asserted utility is not specific or substantial. The specification discloses nothing specific or substantial about LGR-7's amino terminal ectodomain or LGR-7's hormone ligand. Since these asserted utilities are not present in mature form, so that they could be readily used in a real world sense, the asserted utilities are not substantial. Furthermore, the specification of the instant application teaches that LGR-7 has a transmembrane segment and extra-cellular region similar to those of LHR, TSHR, and FSHR (pg 3 lines 26-30). However, there is no disclosure in the specification or the prior art of the structural and functional similarities between LGR-7 and LHR, TSHR, FSHR, or other LGR-type family members. Hsu et al. 2000 teaches that LGR-7 only shares about 24% identity with LHR, TSHR, and FSHR (pg 1258; col 2, paragraph 2). Exhibits 2-4 submitted with the response of 22 October 2003 also do not clearly indicate any strong sequence similarity between domains contained in LGR-7 and domains contained in LHR and TSHR. Finally, although Hsu et al. 2002 demonstrates that LGR-7's ligand is relaxin, this utility is not asserted in the specification as originally filed.

Claims 1-2, 4, 8-11, and 18-20 are also rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Applicant's arguments have been fully considered but are not found to be persuasive. The specification does not teach the functional characteristics of LGR-7 or any polynucleotide variants. Additionally, the problem of predicting protein and DNA structure from sequence data and in turn utilizing predicted structural determinations to ascertain functional aspects of the protein and DNA is extremely complex. Certain positions in the amino acid sequence are critical to the protein's structure/function relationship, e.g. such as various sites or regions directly involved in binding, activity, and in providing the correct three-dimensional spatial orientation of binding and activ sites. These regions can tolerate only relatively conservative substitutions or no substitutions. Applicant has provided little or no guidance beyond the mere presentation of sequence data to enable one or ordinary skill in the art to determine, without undue experimentation, the positions in the LGR-7 protein and DNA which are tolerant to change and the nature and extent of changes that can be made in these positions. Additionally, the specification's general discussion of making and screening for variants (pg 9-11) constitutes an invitation to experiment by trial and error. Undue experimentation would be required by the skilled artisan to generate the infinite number of LGR-7 variants recited in the claims and to screen the same for activity. Also, the specification does not teach the detailed structure of LGR-7, particularly its ectodomain. A large quantity of experimentation would be required of the skilled artisan to identify amino acids that could be altered in LGR-7's overall sequence based upon sequence alignments with other LGR-type GPCRs, due to the low sequence identity shared between LGR-7 and other LGR-type GPCRs (for example, LHR, TSHR, FSHR; see Hsu et al. 2000). Therefore, based upon the discussions above concerning the specific examples of structurally similar proteins that have different functions, along with the art's recognition that one cannot rely upon structural similarity alone to determine functionality, the specification fails to teach the skilled artisan how to use the claimed polynucleotides to make biologically active LGR-7 without undue experimentation to determine what the specific biological

activities of the LGR-7 polypeptide and all LGR-7 variants are. Proper analysis of the Wands factors was performed in the previous Office Action.

Claims 1-2, 4, 8-11, and 18-20 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matte which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant's arguments have been fully considered but are not found to be persuasive. Applicant has not provided evidence to demonstrate that the skilled artisan would be able to envision the detailed structure of the *infinite* number of polynucleotides recited in the claims. The description of two LGR7 polynucleotides and polypeptides in the specification of the instant application is not a representative number of embodiments to support the description of an entire genus of functionally equivalent polynucleotides and polypeptides which incorporate all mutants, derivatives, and fragments having at least 80% identity to the nucleic acid sequences of SEQ ID NO: 7 and the amino acid sequences of SEQ ID NO: 8. Therefore, only an isolated nucleic acid molecule consisting of the nucleotide sequence of SEQ ID NO: 7 and an amino acid sequence of SEQ ID NO: 8, but not the full breadth of the claim meets the written description provision of 35 U.S.C. §112, first paragraph. The specification's general discussion of making and screening for variants constitutes an invitation to experiment by trial and error. Such does not constitute an adequate written description for the claimed derivatives.